

Attorney Docket No.: PENN-0754  
Inventors: Scott L. Diamond  
Serial No.: 09/763,982  
Filing Date: April 25, 2001  
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**Amendments to the Specification:**

Please replace the paragraphs beginning at page 17, line 1, with the following rewritten paragraphs:

--For purposes of chemical conjugation, the M9 sequence has been synthesized with a carboxy terminus addition of Gly-Gly-Gly-Cys (SEQ ID NO:19) to give an accessible thiol group provided by the cysteine:

Nuclear Targeting Peptide (NPS) -

NQSSNFGPMKGGNFGGRSSGPYGGGGQYFAKPRNQGGY-GGGC (SEQ ID NO:1)

The K nuclear shuttling domain (KNS) of the hnRNP K protein is a 39 amino acid sequence:

YDRRGRPGDRYDGMVGFSADETWDSAIDTWSPSEWQMAY (SEQ ID NO:4)

**Example 5: Chemical conjugation of nuclear targeting epitopes to cationic scaffolds**

Several different cationic scaffolds that are rich in amine suitable for conjugation reactions and which mediate electrostatic complexation or condensation with plasmid are used. These scaffolds can include: SV40 T antigen NLS (SVT = CGYGPKKKRKVGG (SEQ ID NO:5)), a mutated version of the SV40 T antigen NLS (muT = VKKGKCRPGKGYG (SEQ ID NO:2)), poly-L-lysine (MW 1, 4, and 30-70 kDa), histone H1, and hydrophilic amine-terminated dendrimers (87,340 MW) of small size (8.4 nm) available through Polysciences, Inc. (Warrington, PA). These scaffolds are tested for DNA condensation using a fluorescence quench assay of ethidium bromide labeled plasmid. Synthetic peptides with a C-terminus Gly-Gly-Gly-

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Cys-COOH (SEQ ID NO:19) linked to M9 or KNS are grafted at 1:1 to 3:1 to the activated amine-rich scaffolds. The crosslinker succinimidyl 4-(N-maleimidomethyl)cyclohexane-1 (SMCC, Pierce) is added at a final concentration of 10 mM (at 10% DMSO) to 100 µg amine rich scaffold (pH 7.2, 25°C for 2 hours) to react the SMCC NHS-ester to the primary amine of the scaffold. Excess SMCC and DMSO are removed by sephadex G-15 chromatography. The activated scaffold is conjugated with equimolar or 2 to 3-fold excess of the KNS or M9 peptide at 4°C (16 hours) by maleimide reaction with the SH moiety of the C-terminal cysteine. Individual reaction species are isolated by electroelution or FLPC. Precipitation with this method has not been observed.--